

CLAIMS

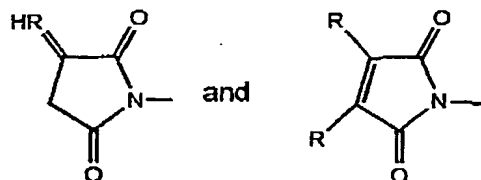
1. A composition comprising a block copolymer having an overall ionic charge and associated with the polymer a biologically active compound having a charge opposite that of the polymer and is characterised in that
5 block copolymer comprises at least one block which has pendant zwitterionic groups and at least one block which comprise ionic groups to confer said overall ionic charge.
2. A composition according to claim 1 in which the biologically active compound is anionic, preferably polyanionic.
- 10 3. A composition according to claim 2 in which where the active compound is a nucleic acid.
4. A composition according to claim 3 in which the nucleic acid is selected from oligo nucleotides, having 5 to 80 bases, single stranded RNA, single stranded DNA and double stranded DNA, preferably plasmid DNA.
- 15 5. A composition according to claim 1 in which the biologically active compound is an anionic drug.
6. A composition according to any preceding claim in which the biologically active compound and polymer are associated with one another in the form of particles having an average diameter less than 200 μm .
- 20 7. A composition according to claim 6 which is an aqueous composition in which the particles are suspended.
8. A composition according to any preceding claim in which the zwitterionic block is formed from ethylenically unsaturated monomers including a zwitterionic monomer having the general formula

25



in which Y is an ethylenically unsaturated group selected from $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4-\text{A}^1-$, $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$, $\text{R}^2\text{O}-\text{CO}-\text{CR}=\text{CR}-\text{CO}-\text{O}$, $\text{RCH}=\text{CH}-\text{CO}-\text{O}-$, $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$,

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5 A is -O- or NR¹;

A¹ is selected from a bond, (CH₂)_lA² and (CH₂)_lSO₃⁻ in which l is 1 to 12;

A² is selected from a bond, -O-, O-CO-, CO-O, CO-NR¹-, -NR¹-CO, O-CO-NR¹-, NR¹-CO-O-;

10 R is hydrogen or C₁₋₄ alkyl;

R¹ is hydrogen, C₁₋₄ alkyl or BX;

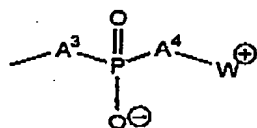
R² is hydrogen or C₁₋₄ alkyl;

B is a bond, or a straight branched alkanediyl, alkylene oxaalkylene, or alkylene (oligooxaalkylene) group, optionally containing one or more
15 fluorine substituents;

X is a zwitterionic group.

9. A composition according to claim 8 in which X is an ammonium, phosphonium, or sulphonium phosphate or phosphonate ester zwitterionic group, more preferably a group of the general formula II

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II

25 in which the moieties A³ and A⁴, which are the same or different, are -O-, -S-, -NH- or a valence bond, preferably -O-, and W⁺ is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is preferably a C₁₋₁₂-alkanediyl group,

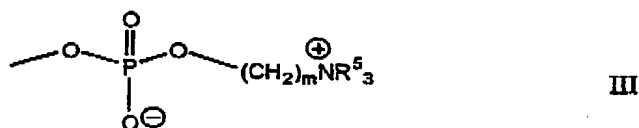
30 preferably in which W⁺ is a group of formula -W¹-N⁺R₃, -W¹-P⁺R₃, -W¹-S⁺R₂ or -W¹-Het⁺ in which:

W¹ is alkanediyl of 1 or more, preferably 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, or alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene or
 5 alkylene cycloalkyl alkylene, which group W¹ optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R³ are the same or different and each is hydrogen or alkyl of 1 to 4 carbon atoms, preferably methyl, or aryl, such as phenyl, or
 10 two of the groups R³ together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or the three groups R³ together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring
 15 structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R³ is substituted by a hydrophilic functional group, and the groups R⁴ are the same or different and each is R³ or a group OR³, where R³ is as defined above; or

Het is an aromatic nitrogen-, phosphorus- or sulphur-, preferably nitrogen-, containing ring, for example pyridine.

20 10. A composition according to claim 8 in which X has the preferred general formula III



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where the groups R⁵ are the same or different and each is hydrogen or C₁₋₄ alkyl, and m is from 1 to 4, in which preferably the groups R⁵ are the same preferably methyl.

11. A composition according to any of claims 8 to 10 in which the
 30 ethylenic unsaturated group Y is H₂C=CR-CO-A-, in which R is preferably hydrogen or methyl and A is preferably NH or, more preferably, O.

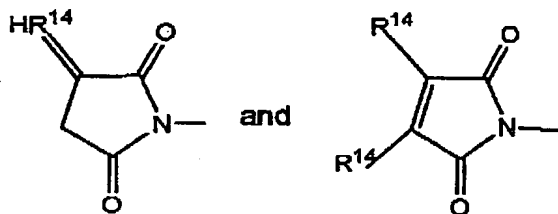
12. A composition according to any of claims 8 to 11 in which the zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.

13. A composition according to any preceding claim in which the ionic block is formed of ethylenically unsaturated monomers including an ionic monomer of general formula VI



VI

in which Y^1 is selected from $H_2C=CR^{14}-CO-A^8$, $H_2C=CR^{14}-C_6H_4-A^9$, $H_2C=CR^{14}-CH_2A^{10}$, $R^{16}O-CO-CR^{14}=CR^{14}-CO-O$, $R^{14}CH=CH-CO-O$, $R^{14}CH=C(COOR^{16})CH_2-CO-O$,



A^8 is $-O-$ or NR^{15} ;

A^9 is selected from a bond, $(CH_2)_qA^{10}$ and $(CH_2)_qSO_3^-$ in which q is 1 to 12;

A^{10} is selected from a bond, $-O-$, $O-CO-$, $CO-O$, $CO-NR^{15}$, $-NR^{15}-CO$, $O-CO-NR^{15}$, $NR^{15}-CO-O$;

R^{14} is hydrogen or C_{1-4} alkyl;

R^{15} is hydrogen, C_{1-4} alkyl or B^1Q ;

R^{16} is hydrogen or C_{1-4} alkyl;

B^1 is a bond, or a straight branched alkanediyl, alkylene oxaalkylene, or alkylene (oligooxalkylene) group, optionally containing one or more fluorine substituents; and

Q is an ionic or ionisable moiety.

14. A composition according to claim 13 in which Q is selected from groups having the formula $-NR^{17}_p$, $-PR^{17}_p$ and SR^{17}_r in which p is 2 or 3, r is 1 or 2, the groups R^{17} are the same or different and each is selected from the

group consisting of hydrogen, C₁₋₂₄ alkyl and aryl, or two of the groups R¹⁷ together with the heteroatom to which they are attached from a 5 to 7 membered heterocyclic ring or three R¹⁷ groups together with the heteroatom to which they are attached form a 5 to 7 membered heteroaromatic ring,

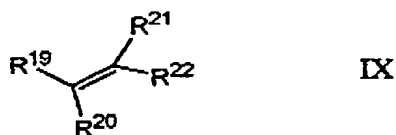
5 either of which rings may be fused to another 5 to 7 membered saturated or unsaturated ring, and any of the R¹⁷ groups may be substituted by amino or hydroxyl groups or halogen atoms.

15. A composition according to claim 14 in which Q is -NR¹⁷₂ where each R¹⁷ is the same and is C₁₋₁₂-alkyl, preferably ethyl.

10 16. A composition according to any of claims 13 to 15 in which B¹ is a C₂₋₈-alkanediyl, preferably (CH₂)₂₋₆.

17. A composition according to claim 8 and/or claim 13 in which the ethylenically unsaturated monomers include comonomer.

15 18. A composition according to claim 17 in which the comonomer has the general formula IX



20 in which R¹⁹ is selected from hydrogen, halogen, C₁₋₄ alkyl and groups COOR²³ in which R² is hydrogen and C₁₋₄ alkyl;

R²⁰ is selected from hydrogen, halogen and C₁₋₄ alkyl;

R²¹ is selected from hydrogen, halogen, C₁₋₄ alkyl and groups COOR²³ provided that R¹⁹ and R²¹ are not both COOR²³; and

25 R²² is a C₁₋₁₀ alkyl, a C₁₋₂₀ alkoxycarbonyl, a mono- or di-(C₁₋₂₀ alkyl) amino carbonyl, a C₆₋₂₀ aryl (including alkaryl) a C₇₋₂₀ aralkyl, a C₆₋₂₀ aryloxycarbonyl, a C₁₋₂₀ -aralkyloxycarbonyl, a C₆₋₂₀ arylamino carbonyl, a C₇₋₂₀ aralkyl-amino, a hydroxyl or a C₂₋₁₀ acyloxy group, any of which may have one or more substituents selected from halogen atoms, alkoxy, oligo-alkoxy, 30 aryloxy, acyloxy, acylamino, amine (including mono and di-alkyl amino and trialkylammonium in which the alkyl groups may be substituted), carboxyl,

sulphonyl, phosphoryl, phosphino, (including mono- and di- alkyl phosphine and tri-alkylphosphonium), zwitterionic, hydroxyl groups, vinyloxy carbonyl and other vinylic or allylic substituents, and reactive silyl or silyloxy groups, such as trialkoxysilyl groups;

5 or R^{22} and R^{21} or R^{22} and R^{20} may together form $-\text{CONR}^{24}\text{CO}$ in which R^{24} is a C_{1-20} alkyl group.

19. A composition according to any preceding claims in which at least one of the blocks has a polydispersity of molecular weight less than 2.0, preferably in the range 1.1 to 1.4.

10 20. A composition according to any preceding claim in which the degree of polymerisation of the ionic block is in the range 5 to 2000, preferably 10 to 250, and the degree of polymerisation of the zwitterionic block is in the range 2 to 1000, preferably 5 to 100, and in which the ratio of the degrees of polymerisation (ionic:zwitterionic) is in the range 1:5 to 10:1, preferably 1:1
15 to 5:1.

21. A composition according to any of preceding claim in which at least one of the blocks is formed by a living radical polymerisation process, preferably a group or atom transfer polymerisation process.

22. A composition according to any preceding claim in which the relative
20 amounts of biologically active compound and polymer are in the range 1:5 to 10:1, preferably 1:2 to 5:2 based on equivalents of the polymer to active compound charged groups.

23. Process for producing a composition according to claim 1 in which an aqueous dispersion of a block copolymer having an overall ionic charge and
25 comprising at least one block which has pendant zwitterionic groups and at least one block which comprise ionic groups to confer said overall ionic charge, is contacted with a biologically active compound having a charge opposite that of the block copolymer, to form an aqueous suspension of block copolymer and associated active.

30 24. Process according to claim 23 in which the average particle size of the suspension is less than 200nm.

25. Process according to claim 23 or claim 24 in which the ratio of equivalents of ionic groups in the block copolymer to ionic groups in the biologically active compound is in the range 10:1 to 1:5, preferably 2:1 to 2:5.

5 26. A process according to any of claims 23 to 25 in which the biologically active is in solution form in an aqueous vehicle when it is contacted with the block copolymer dispersion.

27. A process according to any of claims 23 to 26 having the further features of any of claims 2 to 5 and 7 to 21.